REMARKS

The present application is directed to pharmaceutical compositions containing combinations of antibody fragments and methods of treatment using the compositions for various conditions and in particular in the treatment of conditions caused by toxins.

Claims 1-18 are currently pending in the application. Claims 19 and 21 were withdrawn without prejudice by a previous amendment, and Claims 20 and 22 were previously cancelled.

Rejection under 35 U.S.C. §112

In the Office Action dated September 24, 2007, the Examiner rejected Claims 1-18 under 35 U.S.C. §112, first paragraph, stating that although the claims are enabling for a pharmaceutical composition comprising a large and a small binding fragment of an antibody that binds Botulinum toxin, they are not reasonably enabling for any toxin.

Applicants respectfully disagree and submit that the composition is enabled and effective against all toxins, not just Botulinum toxin. In support of this assertion, applicants refer to the Declaration Under 37 CFR 1.132 of Jane Louise Holley, submitted herewith. The data submitted in the Declaration clearly show that the claimed composition is not only effective against Botulinum toxin, but also against toxins of a different origin and against toxins which have different toxic mechanisms.

For example, applicants refer to Figures S1 and S2 of Dr. Holley's Declaration. These Figures were generated using similar experimental procedures to those described in Examples 1 and 2 of the present application (see page 9, line 19, through page 11, line 13 of the present specification). Figure S1 is a graph of weight loss (as a percentage of animal starting weight) as a function of time after intraperitoneal exposure to 1 μg of ricin and subsequent treatment with the claimed antitoxin compositions at two hours after exposure to ricin. As stated in paragraph 4 of the Declaration, these data show that

throughout the 14 days of the experiment, the animals that were treated with a composition containing a large binding fragment and a small binding fragment of anti-ricin antibodies in accordance with the claims of the present application experienced less weight loss than those animals treated with a large binding fragment of an anti-ricin antibody alone.

Figure S2 is a graph of mean symptom scores of infected animals (using a similar symptom scoring system as described in Example 1 of the present application) as a function of time post-intraperitoneal challenge with ricin toxin. The animals were treated with two different pharmaceutical compositions at two hours post-exposure to ricin and monitored for signs of intoxication for 14 days. As stated in paragraph 5 of Dr. Holley's Declaration, these data clearly show that, on average, animals treated with a composition comprising a large binding fragment of an antibody together with a small binding fragment of an anti-ricin antibody in accordance with the claims of the present application were less susceptible to the visible signs of intoxication than those animals treated with large binding fragments alone.

Thus, it is clear from the data presented in the enclosed Declaration that the claimed composition is effective in treating ricin poisoning and is more effective than using single antibody fragments in terms of improved weight loss and intoxication characteristics. Furthermore, as specified in paragraph 7 of the Declaration, applicants wish to note that Botulinum toxin and ricin toxin have different origins and operate using different toxic mechanisms. As would be known to one skilled in the art of the present application, Botulinum toxin is a neurotoxin, derived from the Gram positive bacterium *Clostridium botulinum*, and is known to block neurotransmitter release at peripheral cholinergeic nerve terminals. Ricin toxin, on the other hand, is derived from the castor oil plant, *Ricinus communis*, and is a potent cytotoxin which inhibits cellular protein synthesis.

Therefore, applicants respectfully submit that the data provided herein, together with the examples in the present application, clearly demonstrate that the claimed composition is effective against toxins of different origins having different modes of action

in the intoxicated subject. The data clearly show that a composition comprising a large binding fragment of an anti-toxin antibody together with a small binding fragment of an anti-toxin antibody in accordance with the claims of the present application provides not only improved protection but a better quality of protection over compositions comprising single antibodies or fragments such as the compositions described in the articles cited by the Examiner in the Office Action (Vaz *et al.* (*MIRCEN Journal*, 1988, filed in IDS) and Ismail *et al.* (*Toxicon*, 1998, filed in IDS)).

The fact that the claimed composition is effective for the treatment of effects from both plant and bacterially-derived toxins with different modes of action indicates that the composition is effective against a wide variety of toxins. In light of the submitted data and the above arguments, applicants respectfully submit that the rejection under 35 U.S.C. §112 has been overcome and request its withdrawal.

Rejection under 35 U.S.C. §102(e)

In the Office Action dated September 24, 2007, the Examiner rejected Claims 1-4 and 6-18 under 35 U.S.C. §102(e) as anticipated by Pomato *et al.* (U.S. 2005/0042775, hereinafter "Pomato").

Applicants respectfully assert that Pomato is not a valid prior art reference under 35 U.S.C. §102(e). Pomato was filed on May 19, 2004 and was not published until February 24, 2005. Although the present application was filed on August 17, 2006, it claims priority to PCT/GB04/02351, which was filed on June 3, 2004, as well as to UK Application 0312642.3, filed on June 3, 2003 (enclosed). Applicants were fully in possession of the claimed invention at the time that UK Application 0312642.3 was filed, (for example, see page 1, lines 30-35, or page 8, lines 8-13, of UK Application 0312642.3). Consequently, the claims of the present application are entitled to a priority date of **June 3, 2003**. Therefore, Pomato is not a valid prior art reference under 35 U.S.C. §102(e).

For the foregoing reasons, applicants respectfully assert that the rejection under 35 U.S.C. 102(e) has been overcome and request its withdrawal.

Rejection under 35 U.S.C. §103(a)

In the Office Action dated September 24, 2007, the Examiner rejected Claim 5 under 35 U.S.C. §103(a) as obvious over Pomato (see above) in view of Stockwin *et al.* (*Biochem Soc Trans*, 2003, Vol. 31, p. 433-6). Applicants respectfully assert that because Pomato is not a valid prior art reference, as discussed above, this rejection has been overcome.

Therefore, applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §103(a).

CONCLUSION

This response fully addresses the rejections in the Office Action of September 24, 2007. In light of the above remarks, applicants respectfully assert that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or if there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 745-2473 is respectfully solicited.

No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

/jamie greene/

By: Jamie Greene
Reg. No. 32,467

KILPATRICK STOCKTON LLP
Suite 2800
1100 Peachtree Street
Atlanta, Georgia 30309-4530
Telephone: 404-815-6500
Facsimile: 404-541-3435
Our Docket: 41577-323890 (P1362)